In the Specification

Page 8, line 19, delete "1994)," and substitute --1994, now U.S. Patent No. 5,919,452),-- therefor. C1

Page 12, line 16, delete "1994)," and substitute --1994, now U.S. Patent No. 5,919,452),-- therefor. C2

Page 17, line 16, delete "1994)," and substitute --1994, now U.S. Patent No. 5,919,452),-- therefor. C3

Page 32, line 30, delete "1994)," and substitute --1994, now U.S. Patent No. 5,919,452),-- therefor. C4

REMARKS

The Examiner's withdrawal of the rejections made in Paper No. 15 under 35 U.S.C. § 112, first and second paragraphs, is acknowledged with appreciation.

Applicants' remarks are set forth below with reference to the numbered paragraphs in the Office Action.

Paragraphs 7 and 8: Rejections of Claims 6, 8-10, 12-15, 29-32 and 34-37 Under 35 U.S.C. §§ 102(b) and 102(e)

Claims 6, 8-10, 12-15, 29-32 and 34-37 have been rejected under 35 U.S.C. § 102(b) as being anticipated by WO92/16553 as evidenced by Wolfe *et al.* (*Arthritis Rheumatism*, 4:481-494 (1994)). Claims 6, 8-10, 12-15, 29-32 and 34-37 have also been rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,698,195 (hereinafter referred to as "the '195 patent") as evidenced by the Wolfe *et al.* reference. In the former rejection, the Examiner alleges that:

> WO92/16553 discloses a method of treatment [of rheumatoid arthritis] comprising the administration of chimeric anti-TNFα antibodies that is the same as that claimed (see, for example, claims 40-41, 3-5, 10, 19). . . . "Treating or preventing thrombosis" (claim 6) and "decreasing plasma fibrinogen" (claim 29) are interpreted as being inherent with the administration of the chimeric anti-TNFα antibodies. As evidenced by Wolfe et al, due to "the large excess of deaths attributable to cardiovascular and cerebrovascular diseases" noted in rheumatoid arthritis patients, they qualify as the "individual in need thereof" of "treating or preventing thrombosis" of claim 6 and the "individual suffering from or at risk of thrombosis" of claim 29.

A similar assertion was made in support of the latter rejection. Applicants respectfully disagree that Claims 6, 8-10, 12-15, 29-32 and 34-37 are anticipated by WO92/16553 or by the '195 patent.

The Court of Appeals for the Federal Circuit has stated that "[u]nder 35 U.S.C. § 102, anticipation requires that each and every element of the claimed invention be disclosed in a prior art reference." Akzo N.V. v. International Trade Comm., 11 U.S.P.Q.2d 1241, 1245 (Fed. Cir. 1986) (citations omitted). An inherent result or characteristic must necessarily flow from the teachings of the prior art. The court has stated that the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993); and In re Oelrich, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

Claims 6, 8-10 and 12-15 relate to methods of treating or preventing thrombosis in a patient in need thereof comprising administering a therapeutically effective amount of a TNF antagonist to the individual. Claims 29-32 and 34-37 relate to methods of decreasing plasma fibrinogen in an individual suffering from or at risk of thrombosis comprising administering a therapeutically effective amount of a TNF antagonist to the individual.

It is noted that both WO92/16553 and the '195 patent claim priority to U.S. Application No. 07/670,827, filed March 18, 1991. Both WO92/16553 and the '195 patent teach cA2 antibodies and antibodies which recognize an epitope containing amino acid residues 87-108 or 59-80 of hTNFα. Both WO92/16553 and the '195 patent teach that the anti-TNF antibodies disclosed therein are useful for treating TNFα-related pathologies, including acute and chronic immune and autoimmune pathologies, such as rheumatoid arthritis (see WO92/16553, e.g., at page 34, lines 3-8, 13-15 and claims 40-41; '195 patent, e.g., at col. 34, lines 32-39, 51-53 and the claims). Guidelines for route of administration and dosages of anti-TNF antibodies to administer in treating TNFα-related pathologies, including acute and chronic immune and autoimmune pathologies, such as rheumatoid arthritis, are provided in the cited references (see WO92/16553, e.g., at page 35, line 7 to page 36, line 7; and '195 patent, e.g., at col. 36, line 5 to col. 37, line 13). Neither WO92/16553 nor the '195 patent provides guidelines for route of administration and dosages of TNF antagonists to administer in treating or preventing thrombosis in a patient or in decreasing plasma fibrinogen in an individual suffering from or at risk of thrombosis. Accordingly, neither WO92/16553 nor the '195 patent discloses, explicitly or inherently, the methods as set forth in Claims 6, 8-10, 12-15, 29-32 and 34-37 of the instant

application (i.e., methods of treating or preventing thrombosis in a patient in need thereof or methods of decreasing plasma fibrinogen in a patient suffering from or at risk of thrombosis, comprising administering a therapeutically effective amount of a TNF antagonist to the patient). Accidental or unwitting duplication of an invention cannot constitute an anticipation. In re Marshall, 198 U.S.P.Q. 344, 346 (C.C.P.A. 1978). Therefore, Claims 6, 8-10, 12-15, 29-32 and 34-37 are not anticipated by WO92/16553 or by the '195 patent.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §§ 102(b) and 102(e) are respectfully requested.

CONCLUSION

In view of the above remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (781) 861-6240.

Respectfully submitted,

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